IN THE SPECIFICATION

Please amend the specification without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows:

Page 2, paragraph beginning on line 15, please amend as follows:

In particular, the nucleotide sequence may be analysed for one or more positions corresponding to positions 62, 78-86, 138, 139, 144, 198, 204, 211, ~~281~~ 218, 240, 249, 300, 321, 419, 429, 437, 457, 466, 486, 602, 606, 627, 636, 645, 803, 971, 1026, 1044, 1173, 1194, 1251, 1278, 1413, 1495, 1500, 1501, 1512, 1518, 1527, 1595, 1611, 1620, 1627, 1629, 1655, 1832, 1856, 1866, 1871, 1892, 1971, 2026, 2088, 2134, 2187 and 2196 as shown in Figure 1.

Page 2, paragraph beginning on line 30 and continuing on page 3, lines 1 and 2, please amend as follows:

We have also shown that a number of surface protein antigen genes, including *rib, alp2* or *alp3* genes, and five mobile genetic elements may be used to molecular subtype GBS. Accordingly, the present invention also provides a method of typing a group B streptococcal bacterium which method comprises determining the presence or absence in the genome of said bacterium of one or more surface protein antigen genes selected from a *rib, alp2* or *alp3* gene, and/or one or more mobile genetic elements selected from IS*861*, IS*1548*, IS*1381*, ISSa*4* and GBSi1. Preferably, ~~such as~~ such a method is combined with the above methods of the invention.

Page 3, paragraph beginning on line 3, please amend as follows:

The nucleotide sequence analysis step may comprise sequencing said one or more regions. Alternatively, or in addition, the nucleotide sequence analysis step may ~~comprises~~ comprise determining whether a polynucleotide obtained from said bacterium selectively hybridises to a polynucleotide probe comprising one or more of the said regions, preferably to one or more of a plurality of polynucleotide probes corresponding to one or more of the said regions.

Page 3, paragraph beginning on line 18, please amend as follows:

In a second aspect, the present invention provides a polynucleotide consisting essentially of at least 10 contiguous nucleotides corresponding to a region within a *cpsD-cpsE-cpsF-cpsG* gene of a group B streptococcal bacterium, said polynucleotide comprising one or more nucleotides which differ between ~~GBS types~~ group B streptococcal serotypes.

Page 3, paragraph beginning on line 23, please amend as follows:

Preferably the nucleotides which differ between GBS types correspond to one or more of positions 62, 78-86, 138, 139, 144, 198, 204, 211, ~~281~~ 218, 240, 249, 300, 321, 419, 429, 437, 457, 466, 486, 602, 606, 627, 636, 645, 803, 971, 1026, 1044, 1173, 1194, 1251, 1278, 1413, 1495, 1500, 1501, 1512, 1518, 1527, 1595, 1611, 1620, 1627, 1629, 1655, 1832, 1856, 1866, 1871, 1892, 1971, 2026, 2088, 2134, 2187 and 2196 as shown in Figure 1.

Page 4, paragraph beginning on line 1, please amend as follows:

The present invention also provides a polynucleotide consisting essentially of at least 10 contiguous nucleotides corresponding to a region within a *cpsI/M* gene of a group B streptococcal bacterium, said polynucleotide comprising one or more nucleotides which differ between group B streptococcal ~~types~~ serotypes.

Page 4, paragraph beginning on line 7, please amend as follows:

The present invention further provides a polynucleotide consisting essentially of at least 10 contiguous nucleotides corresponding to a region within a *rib, alp2* or *alp3* gene of a group B streptococcal bacterium, said polynucleotide comprising one or more nucleotides which differ between ~~GBS protein antigen gene~~ Group B streptococcal subtypes.

Page 8, paragraph beginning on line 14, please amend as follows:

Examples of specific primers/probes which target the *alp2, alp3* and *rib* genes include the following (SEQ ID NOS 23-37, respectively, in order of appearance):

bcaS1 GGT AAT CTT AAT ATT TTT GAA GAG TCA ATA GTT GCT GCA TCT AC

bcaS2 CCAGGGA GTG CAG CGA CCT TAA ATA CAA GCA TC

balS GAT CCT CAA AAC CTC ATT GTA TTA AAT CCA TCA AGC TAT TC

balA CCA GTT AAG ACT TCA TCA CGA CTC CCA TCA C

bal23S1 CAG ACT GTT AAA GTG GAT GAA GAT ATT ACC TTT ACG G

bal23S2 CTT AAA GCT AAG TAT GAA AAT GAT ATC ATT GGA GCT CGT G

~~bal2S~~ bal2S1 CTT CCG CCA GAT AAA ATT AAG

bal2A CTG TTG ACT TAT CTG GAT AGG TC

bal2A1 CGT GTT GTT CAA CAG TCC TAT GCT TAG CCT CTG GTG

bal2A2 GGT ATC TGG TTT ATG ACC ATT TTT CCA GTT ATA CG

~~bal3S~~ bal3S1 GTT CTT CCG CTT AAG GAT AG

bal3A GAC CGT TTG GTC CTT ACC TTT TGG TTC GTT GCT ATC C

ribS2 GAAGTAATTTCAG GAA GTG CTG TTA CGT TAA ACA CAA ATA TG

ribA1 GAA GGT TGT GTG AAA TAA TTG CCG CCT TGC CTA ATG

ribA2 AAT ACT AGC TGC ACC AAC AGT AGT CAA TTC AGA AGG

The primer designations correspond to those given in Table 6.

Page 14, paragraph beginning on line 5, please amend as follows:

Detection of binding of GBS genomic DNA to immobilised probes/primers may be performed using a number of techniques. For example, the immobilised probes which are specific to a number of types (capsular polysaccharide gene serotypes, serosubtypes; protein antigen gene subtypes; mobile ~~genelic elements~~ genetic elements subtypes), may function as capture probes. Following binding of the genomic DNA to the array, the array is washed and incubated with one or more labelled detection probes which hybridise specifically to regions of the GBS genome which are conserved. The binding of these detection probes may then be determined by detecting the presence of the label. For example, the label may be a fluorescent label and the array may be placed in an X-Y reader under a charge-coupled device (CCD) camera.

Page 14, paragraph beginning on line 25, please amend as follows:

A number of available detection techniques do not require labels but instead rely on changes in mass upon ligand binding (e.g. ~~surface plasmon resonance- SPR~~ surface plasmon resonance-SPR). The principles of SPR and the types of solid substrates required for use in SPR (e.g. BIACore chips) are described in Ausubel *et al.*, 1999, supra.

Page 14, paragraph beginning on line 32 and continuing on page 15, lines 1-7, please amend as follows:

As discussed above, group B streptococcus (GBS) - *Streptococcus agalactiae* - is the commonest cause of neonatal and obstetric sepsis and an increasingly important cause of septicaemia in the elderly and immunocompromised patients. Thus, the detection methods, ~~probes/primer~~ probes/primers and microarrays of the invention may be used in the diagnosis of GBS infections in pregnant women, elderly and/or immunocompromised patients. The PCR and microarray techniques described herein may be of particular use in routine antenatal screening of pregnant women as well as in diagnosing infections in pregnant women given the increased accuracy and sensitivity compared to conventional identification and serotyping. These methods are also likely to give faster results since it will not generally be necessary to culture clinical

samples to obtain enough material. Further, the molecular techniques can be used in most laboratories without the need for specialist expertise or reagents.

Page 21, paragraph beginning on line 33, please amend as follows:

There were five isolates belonging to serosubtype III-3, which contained the repetitive sequence and were identical with serosubtype III-1 at three variable sites (139, 144, and 300) and with serosubtype III-2 at four (204,321, 626 and 1629). ~~Seroubtype~~ Serosubtype III-3 differed from both serosubtypes III-1 and III-2 at seven sites (486, 1026, 1413, 1512, 1518, 1527, and 2134). These seven sites in serosubtype III-3 were identical with the corresponding sites of MS Ia.

Table 6 starting on page 58, please amend as follows:

Table 6. Oligonucleotide primers used in this study (SEQ ID NOS 116-143, respectively, in order of appearance).

Primer	**Target gene**	**Tm °C** [1]	**GenBank Accession numbers**	**Sequence** [2, 3]
IgAagGBS[5]	*bac*	73.8	X59771	**2663**GCGATTAAACAA CAA ACT ATT TTT GAT A TTG ACA ATG CAA**2702**
IgAS1[4]	*bac*	72.8	X59771	**2765**GCT AAA TTT CAA AAA GGT CTA GAG ACA AAT ACG CCA G**2801**
IgAA1[4]	*bac*	78.9	X59771	**3157**CCC ATC TGG TAA CTT CGG TGC ATC TGG AAG C**3127**
RigAagGBS[5]	*bac*	76.3	X59771	**3284**CAGCCAACTCTTTC GTC GTT ACT TCC TTG AGA TGT AAC**3247**
GBS1360S[6]	*bac*	72.3	X59771	1325**GTGAAATTGTAT AAG GCT ATG AGT GAG AGC TTG GAG**1360
GBS1717S[4]	*bac*	75.0	X59771	1685**ACA GTC ACA GCT AAA AGT GAT TCG AAG ACG ACG**1717
GBS1937A[6]	*bac*	75.9	X59771	1976**CCGTTTTAGAATCTTT CTG CTC TGG TGT TTT AGG AAC TTG**1937
BcaRUS[7]	*bca* repetitive unit	73.5	M97256	**769**GATAAATATGATCCAA CAG GAG GGG AAA CAA CAG TAC**805**
BcaRUA[7]	*bca* repetitive unit	77.2	M97256	**1003**CTGGTTTTGGTGTCACAT GAA CCG TTA CTT CTA CTG TAT CC**963**

bcaS1[4]	*bca/alp2/alp3*	71.7	M97256 and AF291065	**208/533**GGT AAT CTT AAT ATT TTT GAA GAG TCA ATA GTT GCT GCA TCT AC**251/576**
bcaS2[4]	*bca/alp2/alp3*	78.0	M97256 and AF291065	**256/581**CCAGGGA GTG CAG CGA CCT TAA ATA CAA GCA TC**288/613**
bcaS[4]	*bca*	58.9	M97256	**370**GTT TTA GAA CAA GGT TTT ACA GC**392**
balS[4]	*alp2/alp3*	73.8	AF291065	**677**GAT CCT CAA AAC CTC ATT GTA TTA AAT CCA TCA AGC TAT TC**717**
bcaA[4]	*bca*	74.2	M97256	**597**CGTTCTAACTT CTT CAA TCT TAT CCC TCA AGG TTG TTG**560**
balA[4]	*alp2/alp3*	73.6	AF291065	**978**CCA GTT AAG ACT TCA TCA CGA CTC CCA TCA C**948**
bal23S1[4]	*alp2/alp3*	70.9	AF208158 and AF291065	**1093/1373**CAG ACT GTT AAA GTG GAT GAA GAT ATT ACC TTT ACG G**1129 /1409**
bal23S2[4]	*alp2/alp3*	72.9	AF208158 and AF291065	**1174/1454**CTT AAA GCT AAG TAT GAA AAT GAT ATC ATT GGA GCT CGT G**1213/1493**
~~bal2S[4]~~ bal2S2[4]	*alp2*	59.2	AF208158	**1363**GTT CTT CCG CCA GAT AAA ATT AAG**1386**
bal2A[4]	*alp2*	58.3	AF208158	**1576**CTG TTG ACT TAT CTG GAT AGG TC**1554**
bal2A1[4]	*alp2*	78.3	AF208158	**1426**CGT GTT GTT CAA CAG TCC TAT GCT TAG CCT CTG GTG**1391**
bal2A2[4]	*alp2*	70.8	AF208158	**1518**GGT ATC TGG TTT ATG ACC ATT TTT CCA GTT ATA CG**1484**
~~bal3S[4]~~ bal3S2[4]	*alp3*	57.1	AF291065	**1643**GTT CTT CCG CTT AAG GAT AGC A**1664**
bal3A[4]	*alp3*	79.2	AF291065	**1693**GAC CGT TTG GTC CTT ACC TTT TGG TTC GTT GCT ATC C**1657**
#ribS1[4]	*rib*	65.2	U58333	**216**TAC AGA TAC TGT GTT TGC AGC TGA AG**241**
ribS2[4]	*rib*	73.0	U58333	**238**GAAGTAATTTCAG GAA GTG CTG TTA CGT TAA ACA CAA ATA TG**279**
ribA1[4]	*rib*	78.8	U58333	**431**GAA GGT TGT GTG AAA TAA TTG CCG CCT TGC CTA ATG**396**
ribA2[4]	*rib*	72.6	U58333	**462**AAT ACT AGC TGC ACC AAC AGT AGT CAA TTC AGA AGG**427**
#ribA3[4]	*rib*	61.3	U58333	**570**CAT CTA TTT TAT CTC TCA AAG CTG AAG**554**

Notes.

#For sequencing use only, not entirely specific for rib gene.

1. The primer Tm values are provided by the primer synthesiser (Sigma-Aldrich).
2. Numbers represent the numbered base positions at which primer sequences start and finish (numbering start point "1" refer to the start point "1" of corresponding GenBank accession number, of which there are two for some sequences).
3. Underlined sequences show bases added to modify previously published primers.
4. Primers designed by us for this study.
5. Mawn *et al.*, 1993.
6. Maeland *et al.*, 1997.
7. Maeland *et al.*, 2000.